Ring opening reactions of *N*-substituted-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamides

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Received November 2, 1981

MARSHALL KULKA and W. A. HARRISON. Can. J. Chem. **60**, 1101 (1982).

The amides prepared from 5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl chloride **2** and imidamides **4**, carbamimidothioates **4**, 2-benzimidazolamine **7**, 2-benzothiazolamine **12**, and 2-thiazolamine have been studied. The reaction of **2** with imidamides **4** and with carbamimidothioates **4** in the presence of base gave the amides **5**, which when heated in toluene underwent the 1,4-oxathiin ring opening and rearrangement to produce 2-substituted-5-[(2-hydroxyethyl)thio]-6-methyl-4(1*H*)-pyrimidinones **6**. Acylation of 2-benzimidazolamine **7** with **2** yielded the amide **10**. This, in boiling ethanol, ring opened and rearranged to give the compound **11**. The reaction of 2-benzothiazolamine **12** with **2** gave the rearrangement product **14** directly and neither of the possible amides **13** and **15** could be detected. The amide **15** was synthesized by an unambiguous route from 2-aminobenzenethiol and 5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl isothiocyanate **3**. It would not undergo ring opening and rearrangement when heated. Acylation of 2-thiazolamine with **2** yielded a mixture from which the amide **19** and the rearrangement ester **18** were separated. Structural assignments are based mainly on nmr, uv, and ir spectral evidence.

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On a étudié les amides préparés à partir du chlorure de dihydro-5,6 méthyl-2 oxathiine-1,4 carbonyle-3 (**2**) et des imidamides **4**, des carbamimidothioates **4**, de la benzimidazolamine-2 (**7**), du benzothiazolamine-2 (**12**) et de la thiazolamine-2. Le composé **2** réagit avec les imidamides **4** et avec les carbamimidothioates **4** en milieu basique en donnant les amides **5**, qui par chauffage dans le toluène, subissent une ouverture du cycle oxathium-1,4 et se transposent en donnant les [(hydroxéthyl-2) thio]-5 méthyl-6 (1*H*)-pyrimidinones-4 (**6**) substitués en position 5. L'acylation de la benzimidazolamine-2 (**7**) avec le composé **2** donne l'amide **10**. Ce dernier dans l'éthanol bouillant subit une ouverture de cycle et une transposition qui conduisent au composé **11**. La benzo-2 thiazolamine **12** réagit avec le composé **2** en donnant le produit de transposition **14** directement et on n'a pas pu déceler les amides **13** et **15** qu'il serait possible d'obtenir. On a synthétisé l'amide **15** selon une méthode non équivoque à partir de l'amino-2 benzènethiol et de l'isothiocyanate de dihydro-5,6 méthyl-2 oxathiine-1,4 carbonyle **3**. Le chauffage de ce composé ne provoque pas d'ouverture de cycle ni de transposition. L'acylation de la thiazolamine-2 avec le composé **2** donne un mélange à partir duquel on isole l'amide **19** et l'ester **18** résultant d'une transposition. On a attribué les structures en s'appuyant principalement sur les spectres de rmn, uv et ir.
[Traduit par le journal]

The discovery in 1966 (1) of the systemic fungicides 5,6-dihydro-2-methyl-*N*-phenyl-1,4-oxathiin-3-carboxamide (VITAVAX®) and its 4,4-dioxide (PLANTVAX®),[1] now used throughout the world to control fungal plant pathogens, has created a great deal of interest in the biological activity and the chemistry of 1,4-oxathiins.

Publications (2, 3) from this laboratory record studies of ring opening reactions of *N*-substituted-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamides of the type **1** where X = O and Y = NHR (2), where X = S and Y = NHR (3), and where —C(=X)Y equals 2-pyridyl and 2-pyrimidinyl. In each case, the ring-opening reaction takes place through an attack at the 2-position of the 1,4-oxathiin ring by the nitrogen function followed by rearrangement to form 4(1*H*)-pyrimidinone derivatives.

This paper describes the ring-opening and rearrangement reactions of *N*-substituted-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamides of the type **1** where X = NH and Y = alkyl, aryl, alkylthio, and aralkylthio and where —C(=X)Y is 2-benzimidazolyl, 2-benzothiazolyl, and 2-thiazolyl.

Acylation of 2,2,2-trichloroethanimidamide (**4**, Y = CCl_3) with 5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl chloride (**2**) in the presence of triethylamine gave the amide **5** (Y = CCl_3) in 80% yield. When the amide **5** (Y = CCl_3) was dissolved in toluene and the solution heated under reflux, the 1,4-oxathiin ring opening and rearrangement occurred to form 5-[(2-hydroxyethyl)thio]-6-methyl-2-(trichloromethyl)-4(1*H*)-pyrimidinone (**6**, Y = CCl_3). The amides **5** prepared from **2** and the hydrochlorides of benzeneethanimidamide (**4**, Y = phenylmethyl), benzenemethanimidamide (**4**, Y = phenyl), ethanimidamide (**4**, Y = methyl), and butanimidamide (**4**, Y = propyl) in the presence of aqueous sodium hydroxide were sensitive to heat and no attempts were made to purify them. Instead the crude products were heated in toluene to form the 4(1*H*)-pyrimidinones **6** where Y = phenylmethyl, phenyl, methyl, and propyl respectively. The structural assignments were based on the elemental analysis and on the ir and nmr spectra. It

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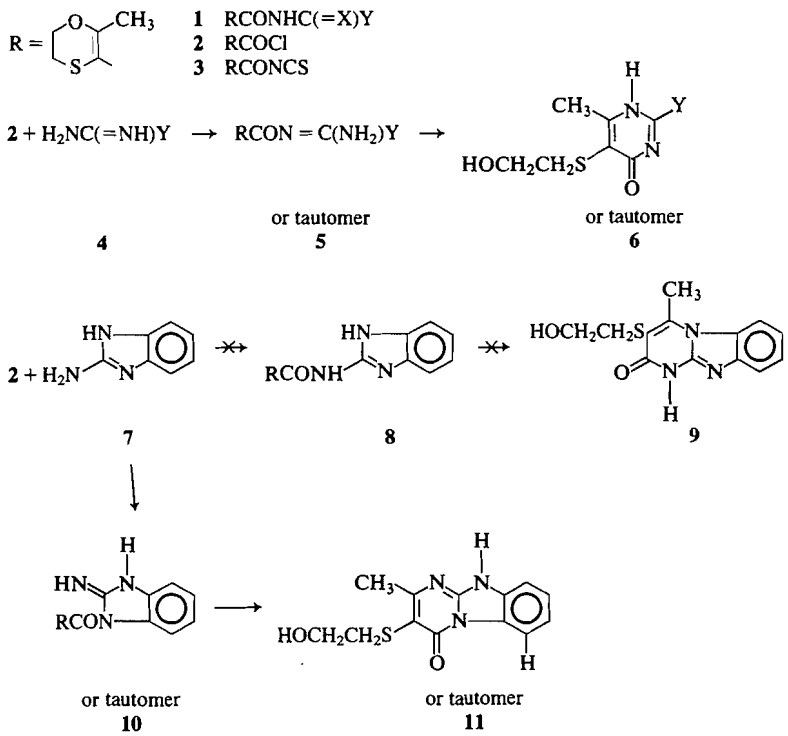

is believed that the compounds **5** exist predominantly in the amino form (RCON=C(NH_2)Y) in view of the fact that their uv spectra are similar to that of *N*-(1-aminoethylidene)benzamide (**5**, R = phenyl, Y = methyl) which exists in the amino form (4).

5,6-Dihydro-*N*[[(2-chlorophenyl)methylthio]-aminomethylene]-2-methyl-1,4-oxathiin-3-carboxamide (**5**, Y = 2-chlorophenylmethylthio), prepared from **2** and the hydrochloride of 2-chlorophenylmethyl carbamimidothioate (**4**, Y = 2-chlorophenylmethylthio), appeared to be stable and could be recrystallized from boiling methanol. However, when it was heated on the steam bath in toluene it quickly underwent the ring-opening and rearrangement reaction to form the 4(1*H*)-pyrimidinone **6** (Y = 2-chlorophenylmethylthio). Similarly, six other amides **5** (Y = 4-chlorophenylmethylthio, phenylmethylthio, 4-nitrophenylmethylthio, 4-methoxy-3-nitrophenylmethylthio, 1-(2,5-dimethylphenyl)-ethylthio, and 2-methyl-2-propenylthio) were prepared and rearranged to the corresponding **6**. An attempt to rearrange 5,6-dihydro-2-methyl-*N*-[[(1-methylethyl)thio]aminomethylene]-1,4-oxathiin-3-carboxamide (**5**, Y = 1-methylethylthio) to the corresponding 4(1*H*)-pyrimidinone **6** was not successful.

The tautomeric forms of 2-benzimidazolamine (**7**) on acylation with **2** could lead to two amides **8** and **10**, which might undergo the 1,4-oxathiin ring opening and rearrangement to yield the pyrimidinones **9** and **11** respectively. Actually, when 2-benzimidazolamine (**7**) was treated with **2** in the presence of triethylamine only one compound could be isolated (in 70% yield). To this compound was assigned the structure **10**, not **8**, on the basis of the following evidence. In boiling ethanol it quickly changed to a less soluble compound to which the rearrangement structure **11** was assigned. This assignment is based on the fact that the aromatic proton in the 6 position of the nmr spectrum shows a shift of almost 1 ppm downfield from the other aromatic protons. This shift is attributed to the deshielding effect of the 6-proton by the keto group of the 4-pyrimidinone **11**, whereas a similar effect is not possible in the 2-pyrimidinone **9**, which might arise from the amide **8**. The assignments of the structure **11** to the rearrangement product and the structure **10** to the intermediate amide are in agreement with previous assignments (2) to the rearrangement product and its intermediate amide from 2-pyridinamine and **2**.

The reaction of 2-benzothiazolamine (**12**) with **2** yielded only one compound to which the rearrangement structure **14** was assigned on the basis of ir and nmr spectra. Neither of the intermediate amides **13** and **15** could be detected. However, the amide **15** was prepared by an unambiguous route from 2-aminobenzenethiol and 5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl isothiocyanate **3** (3) and this amide (**15**) would not undergo rearrange-

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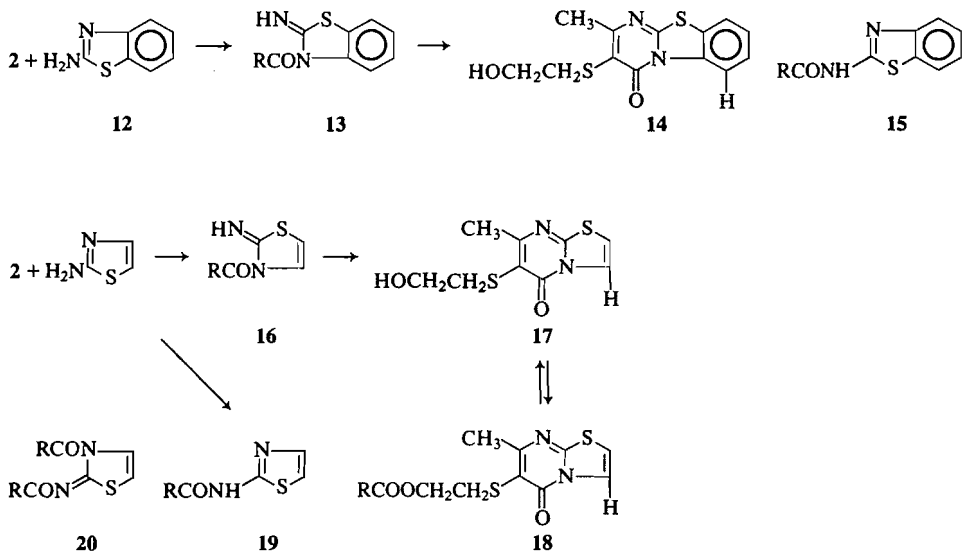

ment even on prolonged heating on the steam bath in toluene in the presence of triethylamine or its hydrochloride. Therefore the amide **15** could not have been the intermediate in the formation of **14**. Further support for the structure **14** comes from the nmr spectra. The aromatic 6-proton is shifted by 1.5 ppm downfield from the other aromatic protons. This is attributed to the deshielding effect by the keto group in the 4-pyrimidinone **14**. A similar effect is not possible in a 2-pyrimidinone structure that might arise from the amide **15**.

The reaction of 2-thiazolamine with the acid chloride **2** was more involved because of the unexpected esterification in addition to the rearrangement reaction. When 2-thiazolamine was treated with **2**, a mixture of two compounds was obtained which was separated by fractional recrystallization from methanol. The more soluble compound was identified as the amide **19** (5, 6) by nmr spectrum, elemental analysis, and by the fact that it was stable and would not rearrange on heating. The less soluble component of the mixture was identified as the ester **18** by elemental analysis, nmr and ir spectra, and by its hydrolysis to the alcohol **17**. The nmr spectra exhibited the aromatic 3-proton shift downfield due to the deshielding of the keto group in not only the ester **18** but also in its hydrolysis product **17**. In another experiment, when 2-thiazolamine was treated with two moles of the acid chloride **2** (instead of one), a 70% yield of the ester **18** was obtained and none of the amide **19** could be isolated. The possibility of the reaction product of 2-thiazolamine and **2** being the bisamide **20** and not the ester **18** was eliminated by evidence from hydrolysis and esterification experiments. Hydrolysis of the ester **18** gave the alcohol **17** which on treatment with **2** gave back the ester **18**. While it is possible that hydrolysis of the bisamide **20** could lead to the alcohol **17** via a rearrangement reaction, the esterification of the alcohol **17** could only lead to the ester **18** and not to the bisamide **20**.

Experimental

The ir spectra were obtained on Perkin–Elmer 237B or 521 grating spectrometers. The nmr spectra were recorded using an R-20 Hitachi Perkin–Elmer spectrometer and are expressed in ppm (δ values) relative to tetramethylsilane as standard. The uv spectra were obtained on a Varian model G34 spectrophotometer. Melting points were determined on a Gallenkamp melting point apparatus and are uncorrected. The elemental analyses were performed on a Perkin–Elmer 240 elemental analyzer.

*5,6-Dihydro-2-methyl-*N*-(2,2,2-trichloro-1-aminoethylidene)-1,4-oxathiin-3-carboxamide (**5**, Y = CCl_3)*

To a solution of 5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl chloride (**2**) (2) (prepared from 12 g of the corresponding acid) in toluene (100 mL) was added triethylamine (10 g) followed by 2,2,2-trichloroethanimidamide (**4**, Y = CCl_3) (12 g) in toluene (50 mL) keeping the temperature of the reaction mixture below 50°C by cooling occasionally. The reaction mixture was allowed to stand overnight and then the triethylamine hydrochloride was filtered off. The filtrate was concentrated *in vacuo* below 50°C to about 50 mL and allowed to cool. The yellow prisms were filtered, washed, and dried, mp 122–124°C, yield 18.1 g or 80%. The melting point was 125–126°C after recrystallization from methanol; uv (CH_3OH) λ_{max}: 212, 277 nm (ε 7018, 4021); ir (KBr): 3400, 3180, 1640 cm^{-1}; nmr ($CDCl_3$) (after standing in $CDCl_3$ solution for 24 h at 34°C): 8.5 (2H, m, NH_2), 4.35 (2H, m, OCH_2), 2.98 (2H, m, SCH_2), 2.50 (3H, m, CH_3) (a tautomeric mixture is indicated in a fresh solution). *Anal.* calcd. for $C_8H_9Cl_3N_2O_2S$: C 31.64, H 2.97, N 9.19; found: C 31.78, H 2.92, N 9.22.

*5-[(2-Hydroxyethyl)thio]-6-methyl-2-(trichloromethyl)-4(1*H*)-pyrimidinone (**6**, Y = CCl_3)*

A solution of 5,6-dihydro-2-methyl-*N*-(2,2,2-trichloro-1-

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aminoethylidene)-1,4-oxathiin-3-carboxamide (**5**, Y = CCl_3) (8 g) in toluene (50 mL) was heated under reflux for 3 h and then allowed to cool overnight. The white prisms were filtered, washed, and recrystallized from toluene, mp 161–162°C, yield 4.5 g or 56%; nmr (DMSO-d_6): 3.55 (2H, m, OCH_2), 3.05 (2H, m, SCH_2), 2.68 (3H, s, CH_3), OH and NH broad. *Anal.* calcd. for $C_8H_9Cl_3N_2O_2S$: C 31.64, H 2.98, N 9.22; found: C 31.91, H 3.01, N 9.17.

*5-[(2-Hydroxyethyl)thio]-6-methyl-2-phenylmethyl-4(1H)-pyrimidinone (**6**, Y = phenylmethyl)*

To a stirred suspension of benzeneethanimidamide (**4**, Y = phenylmethyl) hydrochloride (12 g) in acetone (150 mL) was added portionwise with cooling (below 20°C) a solution of sodium hydroxide (5 g) in water (10 mL). To this reaction mixture was added portionwise with stirring and cooling a solution of the acid chloride **2** (2) (prepared from 10 g of the corresponding acid) in acetone (40 mL) keeping the temperature below 20°C. The reaction mixture was stirred overnight, filtered, and the filtrate distilled *in vacuo*. The residue was extracted with ether, the extract washed with aqueous sodium bicarbonate, and the ether distilled off. The liquid residue was heated on the steam bath for 1 h. The resulting solid product was extracted with dilute hydrochloric acid, the extract filtered, and the filtrate neutralized with solid sodium bicarbonate. The white precipitate was filtered, washed with water, and crystallized from methanol to yield 8.5 g (or 50%) of white crystals melting at 179–180°C; ir (KBr): 3260, 1663 cm^{-1}; nmr (DMSO-d_6): 7.32 (5H, s, aromatic), 3.86 (2H, s, CH_2), 3.46 (2H, m, OCH_2), 2.90 (2H, m, SCH_2), 2.43 (3H, s, CH_3), OH and NH broad. *Anal.* calcd. for $C_{14}H_{16}N_2O_2S$: C 60.86, H 5.84, N 10.14; found: C 60.98, H 5.82, N 10.02.

*5,6-Dihydro-N-[[(2-chlorophenyl)methylthio]amino-methylene]-2-methyl-1,4-oxathiin-3-carboxamide (**5**, Y = 2-chlorophenylmethylthio)*

Solid 2-chlorophenylmethyl carbamimidothioate (**4**, Y = 2-chlorophenylmethylthio) hydrochloride (34 g) was added in portions over 0.5 h to a stirred and ice-cooled (3 to 5°C) solution of the acid chloride **2** (prepared from 22 g of the corresponding acid) in dry toluene (200 mL) and triethylamine (35 g). The stirring was continued at 3 to 5°C for 2 h and then at room temperature overnight. The precipitated triethylamine hydrochloride was filtered and the solvent removed from the filtrate *in vacuo* at room temperature. The residue was dissolved in ether, the solution washed with water, and the ether distilled off. The residue was crystallized from methanol to give light-yellow prisms (28 g or 60%) melting at 105–106°C; uv (CH_3OH) λ_{max}: 215, 268 nm (ε 16 825, 14 085); ir (KBr): 3330, 3240, 1610 cm^{-1}; nmr ($CDCl_3$): 8.05 (2H, s, NH_2), 7.70 (H, m, aromatic), 7.30 (3H, m, aromatic), 4.60 (2H, s, SCH_2), 4.33 (2H, m, OCH_2), 2.95 (2H, m, SCH_2), 2.40 (3H, s, CH_3). *Anal.* calcd. for $C_{14}H_{15}ClN_2O_2S_2$: C 49.04, H 4.41, N 8.16; found: C 49.01, H 4.30, N 8.43.

Other N-[(substituted)-aminomethylene]-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamides prepared, for which analysis, yields, and nmr spectra are available from the Depository of Unpublished Data[2] are **5** where Y = phenylmethylthio, mp 79–80°C; Y = 4-chlorophenylmethylthio, mp 120–121°C; Y = 4-nitrophenylmethylthio, mp 131–133°C; Y = 4-methoxy-3-nitrophenylmethylthio, mp 105–107°C; Y = α,2,5-trimethylphenylmethylthio, mp 109–110°C; Y = 2-methyl-2-propenylthio, liquid, and Y = 1-methylethylthio, mp 101–103°C.

[2]Photocopies may be obtained at a nominal charge upon request from the Depository of Unpublished Data, CISTI, National Research Council of Canada, Ottawa, Ont., Canada K1A 0S2.

*2-[(2-Chlorophenyl)methylthio]-5-[(2-hydroxyethyl)thio]-6-methyl-4(1H)-pyrimidinone (**6**, Y = 2-chlorophenyl)-methylthio)*

A solution of 5,6-dihydro-*N*-[[(2-chlorophenyl]methylthio]-aminomethylene]-2-methyl-1,4-oxathiin-3-carboxamide (**5**, Y = (2-chlorophenyl)methylthio) (16 g) in toluene (12 mL) was heated on the steam bath for 3 h and then allowed to cool. The white solid was filtered and recrystallized from toluene, mp 134–136°C, yield 10 g or 63%; nmr (DMSO-d_6): 7.50 (4H, m, aromatic), 4.50 (2H, s, SCH_2), 3.50 (2H, m, OCH_2), 2.90 (2H, m, SCH_2), 2.52 (3H, s, CH_3), OH and NH broad. *Anal.* calcd. for $C_{14}H_{15}ClN_2O_2S_2$: C 49.04, H 4.41, N 8.16; found: C 49.01, H 4.32, N 8.55.

Other 2-Substituted-5-[(2-hydroxyethyl)thio]-6-methyl-4(1H)-pyrimidinones prepared for which analysis, yields, and nmr spectra are available from the Depository of Unpublished Data[2] are **6** where Y = phenyl, mp 221–223°C; Y = methyl, mp 151–153°C; Y = propyl, mp 141–143°C; Y = phenylmethylthio, mp 144–145°C; Y = 4-chlorophenylmethylthio, mp 172–173°C; Y = 4-nitrophenylmethylthio, mp 187–189°C; Y = 4-methoxy-3-nitrophenylmethylthio, mp 183–184°C; Y = α,2,5-trimethylphenylmethylthio, mp 148–150°C; and Y = 2-methyl-2-propenylthio, mp 128–130°C.

*2,3-Dihydro-3-(5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl)-1H-benzimidazol-2-imine (**10**, R = 5,6-dihydro-2-methyl-1,4-oxathiin-3-yl)*

To a solution of 2-benzimidazolamine (**7**) (6.7 g) in dry acetone (150 mL) and triethylamine (7 g) was added portionwise with stirring a solution of the acid chloride, **2** (prepared from 8.5 g of the corresponding acid), in acetone (25 mL), keeping the temperature below 35°C by occasional cooling. The reaction mixture was stirred for 5 h, cooled to −5°C, filtered, washed with cold acetone and with water, and dried. The white solid weighed 9.7 g (or 70%) and melted at 245–247° dec. Infrared (KBr): 3420, 3100, 1680 cm^{-1}; nmr (DMSO-d_6): 7.15 (4H, m, aromatic); 4.48 (2H, m, OCH_2); 3.18 (2H, m, SCH_2), 1.86 (3H, s, CH_3), 2NH broad. *Anal.* calcd. for $C_{13}H_{13}N_3O_2S$: C 56.72, H 4.76, N 15.27; found: C 56.61, H 5.13, N 14.95.

*3-[(2-Hydroxyethyl)thio]-2-methylpyrimido[1,2-a]benzimidazol-4(10H)-one (**11**)*

A solution of 2,3-dihydro-3-(5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl)-(1*H*)-benzimidazol-2-imine (**10**) (10 g) in 95% ethanol (120 mL) was heated under reflux for 2 h (precipitation began soon after the heating started). The mixture was cooled, filtered, washed, and dried. The white solid (8.5 g or 85%) melted at 254–255° dec. Infrared (KBr): 3400, 1675 cm^{-1}; nmr (DMSO-d_6): 8.43 (1H, m, aromatic), 7.45 (3H, m, aromatic), 3.55 (2H, m, OCH_2), 2.86 (2H, m, SCH_2), 2.62 (3H, s, CH_3), NH and OH broad. *Anal.* calcd. for $C_{13}H_{13}N_3O_2S$: C 56.72, H 4.76, N 15.27; found: C 57.30, H 4.90, N 14.80.

*3-[(2-Hydroxyethyl)thio]-2-methyl-4H-pyrimido[2,1-b]benzothiazol-4-one (**14**)*

A solution of the acid chloride, **2** (prepared from 12 g of the corresponding acid), in toluene (50 mL) was added to a solution of 2-benzothiazolamine (**12**) (10 g) in toluene (100 mL) and triethylamine (12 g). The temperature went up to 45°C. The reaction mixture was allowed to stand overnight. The precipitate was filtered, washed with methanol, with warm water and with methanol, and dried, mp 144–145°C after recrystallization from ethanol, yield 10 g or 45%. The same results were obtained when the reaction was carried out at 0°C. Infrared (KBr): 3425, 1675 cm^{-1}; nmr ($CDCl_3$): 9.05 (H, m, aromatic), 7.55 (3H, m, aromatic), 3.70 (3H, m, OCH_2 and OH), 2.98 (2H, m, SCH_2), 2.70 (3H, s, CH_3); *Anal.* calcd. for $C_{13}H_{12}N_2O_2S_2$: C 53.43, H 4.14, N 9.59; found: C 53.34, H 4.23, N 9.45.

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*N-(2-Benzothiazolyl)-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxamide (**15**)*

To a solution of 5,6-dihydro-2-methyl-1,4-oxathiin-3-carbonyl isothiocyanate (**3**) (3) (prepared from 12 g of the corresponding acid via the acid chloride **2** and ammonium thiocyanate) in dry toluene (100 mL) was added a solution of 2-aminobenzenethiol (9.5 g) in toluene (15 mL). The reaction mixture was heated at 70–80°C for 4 h to liberate the hydrogen sulfide, then concentrated *in vacuo* to about 60 mL and allowed to cool. The precipitate was filtered and recrystallized from ethanol, golden prisms, mp 173–175°C, yield 11.1 g or 50%; nmr ($CDCl_3$): 9.75 (H, m, NH), 7.82 (2H, m, aromatic), 7.35 (2H, m, aromatic), 4.40 (2H, m, OCH_2), 2.90 (2H, m, SCH_2), 2.36 (3H, s, CH_3). This compound remained unchanged when heated in toluene on the steam bath for 3 h in the presence of triethylamine or triethylamine hydrochloride. *Anal.* calcd. for $C_{13}H_{12}N_2O_2S_2$: C 53.43, H 4.14, N 9.59; found: C 53.19, H 4.17, N 9.50.

*5,6-Dihydro-2-methyl-N-(2-thiazolyl)-1,4-oxathiin-3-carboxamide (**19**) and 2-[(7-methyl-5-oxo-5H-thiazolo[3,2-a]pyrimidin-6-yl)thio]ethyl-5,6-dihydro-2-methyl-1,4-oxathiin-3-carboxylate (**18**)*

A solution of the acid chloride (**2**) (prepared from 12 g of the corresponding acid) in toluene (30 mL) was added portionwise to a solution of 2-thiazolamine (8 g) in toluene (120 mL) and triethylamine (15 g), keeping the temperature below 50°C by occasional cooling. The reaction mixture was allowed to stand at room temperature for 2 days and then filtered. The filtrate was taken to "dryness" *in vacuo* and the residue fractionally crystallized from methanol. The more soluble component (2.8 g) melted at 120–122°C after repeated crystallization from toluene (lit. (5) mp 96–98°C and (6) 114–116°C). Infrared (KBr): 3120, 1655 cm^{-1}; nmr ($CDCl_3$): 10.95 (1H, s, NH), 7.45 (1H, m, aromatic), 6.98 (1H, m, aromatic), 4.42 (2H, m, OCH_2), 2.98 (2H, m, SCH_2), 2.25 (3H, s, CH_3). This compound remained unchanged when heated under reflux in toluene in the presence of triethylamine or its hydrochloride. *Anal.* calcd. for $C_9H_{10}N_2O_2S_2$: C 44.63, H 4.16, N 11.57; found: C 44.85, H 4.23, N 11.09.

The less soluble component of the above mixture on recrystallization from methanol and from toluene yielded (1.7 g) the pure ester **18** melting at 140–141°C. In another experiment, when 2-thiazolamine was treated with 2 moles of the acid chloride **2** as above instead of one mole, a 70% yield of the ester **18** was obtained (about half the ester precipitated out of the reaction mixture along with triethylamine hydrochloride). No amide **19** could be found. Infrared (KBr): 1690, 1675 cm^{-1}; nmr ($CDCl_3$): 8.00 (1H, m, aromatic), 7.12 (1H, m, aromatic), 4.30 (4H, m, $2OCH_2$), 3.25 (2H, m, SCH_2), 2.90 (2H, m, SCH_2), 2.68 (3H, s, CH_3), 2.30 (3H, s, CH_3). *Anal.* calcd. for $C_{15}H_{16}N_2O_4S_3$: C 46.88, H 4.20, N 7.29; found: C 46.74, H 4.26, N 7.30.

*6-[(2-Hydroxyethyl)thio]-7-methyl-5H-thiazolo[3,2-a]pyrimidin-5-one (**17**)*

The ester **18** (10 g) was dissolved in boiling ethanol (200 mL), concentrated hydrochloric acid (25 mL) in water (110 mL) added, and the reaction mixture was heated one hour on the steam bath. Concentration of the reaction mixture to 50 mL, *in vacuo*, neutralization with sodium bicarbonate, and extraction with ether yielded 5 g of white crystals melting at 89–91°C after recrystallization from toluene. Infrared (KBr): 3410, 3065, 1650 cm^{-1}; nmr ($CDCl_3$): 8.00 (1H, d, aromatic), 7.25 (1H, d, aromatic), 4.20 (1H, m, OH), 3.68 (2H, m, OCH_2), 2.95 (2H, m, SCH_2), 2.70 (3H, s, CH_3). *Anal.* calcd. for $C_9H_{10}N_2O_2S_2$: C 44.63, H 4.16, N 11.57; found: C 44.69, H 4.09, N 11.58.

This compound (**17**), when treated with the acid chloride **2** and triethylamine, regenerated the ester **18**.

Acknowledgements

Grateful acknowledgements are made to W. R. Boos, Murray Ross, and Helen Van Veggel for providing analyses and nmr, ir, and uv spectra.

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